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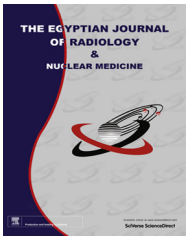

ORIGINAL ARTICLE

# Diagnosis of arterioportal shunts in cases of hepatocellular carcinoma using multidetector CT: Impact on clinical management

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**KEYWORDS**

Multidetector CT;
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Chemoembolization

**Abstract** *Purpose:* To study the ability of multidetector CT (MDCT) to diagnose arterioportal shunts (APS) associated with hepatocellular carcinoma (HCC) and its impact on further management of the patient.

*Patients and methods:* 252 Patients with HCC were examined by triphasic MDCT scanning. Images were analyzed for the presence, locations, types and degrees of APS, being with or without thrombosis. Digital subtraction angiographies (DSA) were performed for 22 patients as a part of further therapeutic management.

*Results:* MDCT revealed APS in 37 patients including 20 central, 9 peripheral and 8 mixed. According to the degree we had 13 severe, 15 moderate and 9 mild APS. 18 patients had associated portal venous thrombosis. During DSA examinations; APS were demonstrated in 19 out of 22 as 3 mild and peripheral shunts were faint and missed. Embolization of the shunt was performed in 17 patients prior to injection of the cytotoxic drug-lipiodol mixture. In one patient the APS was closed to improve the hepatic status without further chemotherapy and in one patient the shunt was ignored and not closed.

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*Conclusion:* Good understanding of MDCT findings of APS complicating HCC contributes to the diagnosis and improves the therapeutic outcome of the chemoembolization procedures.

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## 1. Introduction

Arterioportal shunt (APS) is an organic or functional communication between the high-pressure hepatic arterial branch and low-pressure portal veins (1). Hepatocellular carcinoma (HCC) can easily invade the adjacent portal vein to form the direct communication between the hepatic artery or its branches and portal veins, resulting in arterioportal shunt (APS). Hepatic APS may cause or aggravate portal hypertension and consequently, splenomegaly, bleeding from esophageal varices and hepatic encephalopathy, accelerating intra hepatic dissemination and extra hepatic metastasis of tumor cells (2).

One of the most important lines of palliative treatment of HCC is trans-catheter chemo-embolization (3). The formation of HCC-associated APS may bring some difficulty and danger to the procedure, such as cause chemotherapy drug and embolic agent to run-off through shunt path, and result in aberrant embolism (4). The embolic agent will be diverted to branches of the portal vein and delivered to normal areas of the liver instead of being deposited in the tumor, a problem which can be overcome by super selective embolization of the APS using micro catheters if the condition is diagnosed before treatment (5).

Transcatheter hepatic angiography, including digital subtraction angiography (DSA) is the gold standard for diagnosis of HCC-associated APS, but has the disadvantage of being an invasive procedure (2). Multidetector CT (MDCT) could contribute to the diagnosis of hepatic APS complicating HCC due to its fast scanning and improved image resolution and quality (6). CT hepatic arteriography findings in APS have a major impact on planning the way in which chemoembolization treatment could be performed. Findings of this modality may alter treatment plans for the tumor and the shunts involving selective administration of chemo embolic material (7), so understanding of CT diagnostic criteria of hepatic APS complicating HCC is of significant clinical implications.

The aim of this study was to investigate the ability of multidetector CT (MDCT) to diagnose arterioportal shunt (APS) complicating hepatocellular carcinoma (HCC) and the impact of that on further patient's management.

## 2. Patients and methods

This prospective study was carried out in the Radiodiagnosis Department of Ain Shams University Hospital and in some private centers between February 2011 and January 2013. Multidetector CT was conducted for 252 patients with HCC. They included 214 males and 38 females and their ages ranged between 39 and 75 years. An informed consent was obtained from each patient before the study. The diagnosis of HCC was based on the classical findings of enhancing lesions at the arterial phase with rapid wash out of the contrast at the venous phase, associated with elevated/progressively rising alpha fetoprotein level. Some cases were confirmed by percutaneous needle biopsy.

Helical CT scans were performed using at least 8 slice multi-detector scanners (GE Healthcare, Milwaukee, WI, USA) with a kV of 140, 200–300 mA and 0.8-s gantry rotation time. Most patients were examined after an overnight or 6 h fast, with water (or sometimes gastrografin) being used to mark the stomach and bowel loops. Dynamic CT scans were acquired after the injection of 80–120 cc iodinated contrast medium (Ultravist 300; Schering, Berlin, Germany or Iopamiro 300; Bracco, Milano, Italy) at a pressure of 600 PSI and a rate 4 ml/s using an automatic pump injector (Angiomat 6000; Liebel-Flarsheim) and via an 18- or 20-gauge canula inserted into an antecubital or peripheral upper limb vein. The scans were acquired in the early arterial, late arterial and porto-venous phases after a delay of 15, 25 and 60 s respectively. The patients were not instructed to maintain strict apnea. Instead; they were imaged during gentle shallow breathing.

We used an effective slice thickness of 7 mm and the images were reconstructed at 10 mm intervals to achieve an overlap of 40–50%. The images were then further reconstructed at 1 mm thickness/intervals producing about 150–200 sections per acquisition and sent to workstation (Hp xw 8600, AW Volume share 4, GE medical systems SCS, France) where coronal and sagittal reformats were acquired. Volume rendering techniques were also used particularly the maximum intensity projection (MIP) to demonstrate the small peripheral vessels.

The CT diagnostic criteria for APS were earlier enhancement or stronger opacification of main portal trunk and/or its first-order branches than that of superior mesenteric or the splenic vein; or earlier enhancement or stronger opacification of the second-order and smaller branches of portal veins than that of the main portal trunk (8).

Depending upon the location of shunt, APS were classified into three types: The ***central*** type was the shunt located at the porta hepatis with earlier enhancement and/or stronger opacification of the main portal trunk and/or the first-order branches at the hepatic arterial phase. The ***peripheral*** type was the shunt located in the peripheral liver parenchyma with earlier enhancement and/or stronger opacification of the second order and smaller branches of the portal vein, or transient patchy or wedge-shaped enhancement peripheral to HCC foci at the late hepatic arterial phase. The ***mixed*** type showed both central and peripheral criteria (2).

According to the time of appearance of APS on images, APS were divided into three degrees. The ***severe*** APS showed opacification of the main portal trunk and/or the first-order branches with enhancement of the hepatic artery and its branches at the early hepatic arterial phase, with no or mild enhancement of HCC foci. The ***moderate*** APS demonstrated

opacification of the main portal trunk and/or the first-order branches with middle or late enhancement of HCC foci at the late hepatic arterial phase. The ***mild*** APS revealed opacification of the second-order and smaller branches of the portal veins at the late hepatic arterial phase, with transient patchy or wedge-shaped enhancement peripheral to HCC foci (2).

The interventional procedures were carried out at the interventional radiology units of Ain Shams University hospitals. A femoral arterial approach was used with the Seldinger technique. The hepatic artery was catheterized with a 5F polyethylene catheter with cobra head configuration (C2 Cordis® USA) in 17 cases and a reverse 5F catheter (Simmonds S2, Cordis® USA) in five cases. The catheter was advanced into the proximal hepatic artery and an initial subtracted angiogram was obtained after hand injection of 8 cc of non ionic contrast (Ultravist 300; Schering, Berlin, Germany) to detect the arterioportal fistula. The catheter was further advanced so that the feeding artery of the fistula was super selectively catheterized and embolization was done under fluoroscopic guidance with serial repeated control angiograms. Evidence of successful embolization was defined by complete stasis of the injected contrast and embolizing material. In some cases we used a 3.8 f micro catheter (Renegade, Boston Scientific ® USA).

In cases of mild, moderate or peripheral shunts we used gel foam as the embolizing material, being cut into small pledges and mixed with contrast. In cases of central and severe shunts we used N-butyl-2-cyanoacrylate (Histoacryl®) mixed with lipiodol with a 1:1 ratio.

## 3. Results

MDCT scanning revealed 37 APS in 252 patients with HCC. They were classified according to their location as 20 central, 9 peripheral and 8 mixed, and according to their degree as 13 severe, 15 moderate and 9 mild.

The study included 6 central and severe APS (Fig. 1), 11 central and moderate APS (Fig. 2), 9 peripheral and mild APS (Figs. 3 and 4), 2 mixed and severe APS (Fig. 5) and 7 mixed and moderate APS (Fig. 6). Wedge-shaped enhancement peripheral to HCC foci was noted in 3 patients with mild and peripheral APS (Fig. 7).

MDCT showed that 18 patients with APS also had portal venous thromboses including 4 patients with partial tumoral thrombosis in the main portal vein and total thrombosis in

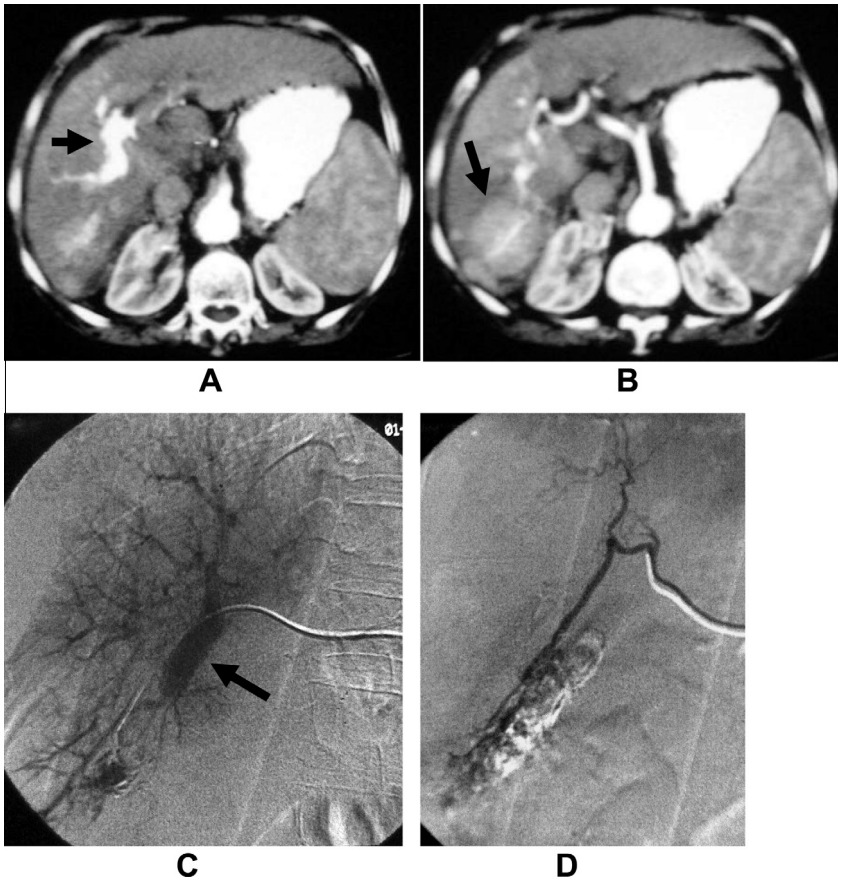


**Fig. 1** Central severe fistula: 56 year old male patient with liver cirrhosis and large posterior right hepatic lobe HCC at segment VI. (A and B) Axial sequential CT cuts show marked enhancement of the right portal vein during the early arterial phase (arrow in A) and the hepatoma (arrow in B). (C) DSA of the right hepatic artery confirms the presence of the fistula with filling of posterior branch of the right portal vein (arrow). (D) Super selective hepatic arteriogram after embolization of the fistula using N-butyl-2-cyanoacrylate (Histoacryl)® with no filling of the right portal vein.

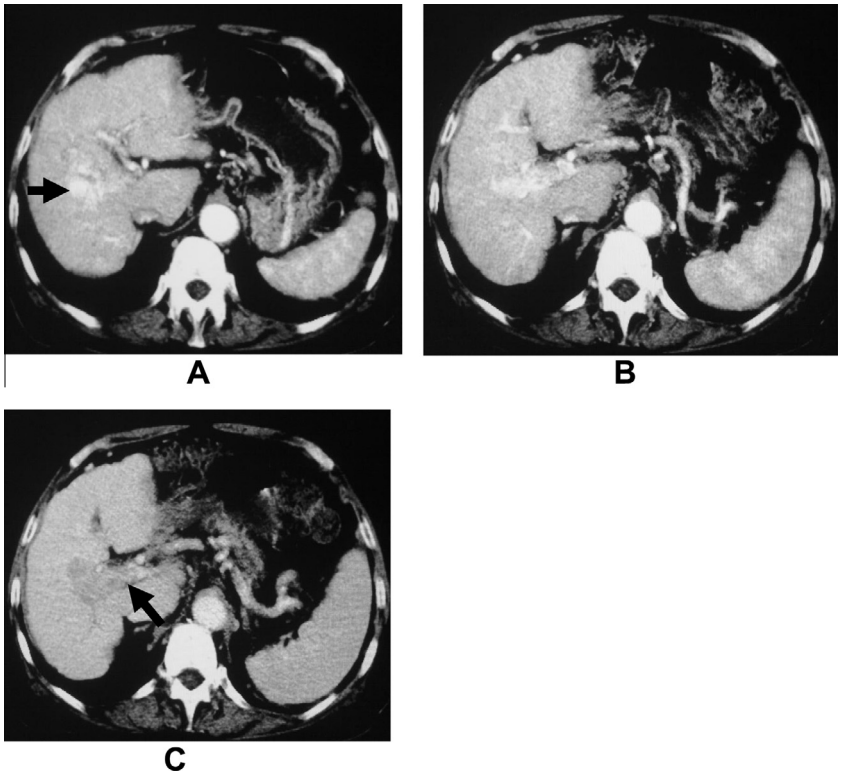


**Fig. 2** Moderate central APS: 67 year old male patient with liver cirrhosis and nodular HCC at the vicinity of the right main portal vein. (A) Axial CT cut at the late arterial phase shows enhancement of the HCC (arrow). (B) More caudal scan shows shunting of the contrast to the right portal vein. (C) Thrombosis of the right portal vein is confirmed at the portal venous phase (arrow). No intervention could be performed and Sorafenib was recommended for further management.

right portal veins, two of them with sectorial differential hypodensity of the right hepatic lobe suggesting infarction (Fig. 8). Six patients had thromboses in the right portal vein (Fig. 6), 5 patients had thrombosis in the proximal part of the left portal vein (Fig. 5), and lastly 3 patients with thrombosis in the distal part of the left portal vein. Accordingly; we had 19 APS patients without portal vein thrombosis.

In most patients with central severe or moderate shunts, the degree of enhancement of the hepatic and splenic parenchyma was relatively decreased.

Depending upon the data obtained from MDCT, DSA was performed for 22 patients who were suitable for chemoembolization, taking into consideration the guidelines of the American Association for the Study of Liver Diseases (AASLD) and Barcelona Clinic of Liver Cancer (BCLC) staging systems (9), and each case was discussed and evaluated individually by a multi-disciplinary tumor board.

DSA showed nineteen out of the twenty-two APS while 3 mild and peripheral APS were faint and missed by DSA.

These 19 APS were managed as follows: Embolization of the shunt was performed in 17 cases prior to injection of cytotoxic drug-lipiodol mixture, one APS was closed only without chemotherapy and the other one was ignored and not closed.

## 4. Discussion

Hepatocellular carcinoma is a leading cause of morbidity and mortality worldwide, accounting for approximately 1 million deaths per year, fueled by the increasing incidence of viral hepatitis (7).

The major etiological factor of liver cancer is hepatitis B virus (HBV), followed by hepatitis C virus (HCV) infection. In Egypt, HBV and HCV are considered major health problems and disease prognosis may be worse in conjunction with schistosomiasis. Accordingly, the incidence of HCC in Egypt is among the highest in the world (10).

Arterioportal shunts are the most common vascular communications associated with advanced HCC (11).

In HCC patients treated with transarterial chemoembolization, hepatic AP shunts may be problematic because chemotherapeutic agents go through the shunts and may cause systemic toxicity as well as decrease the chemotherapeutic effects against the tumor (12).

Trans-catheter hepatic angiography has been the gold standard for diagnosis of APS in the past and can reveal the shunt locations, types and degrees. However, it is an invasive examination and may fail due to anatomic variations of the hepatic artery. Also mild and peripheral APS may be missed because of unsatisfactory opacification of the hepatic artery or faint shunt especially when associated with massive HCC (2).

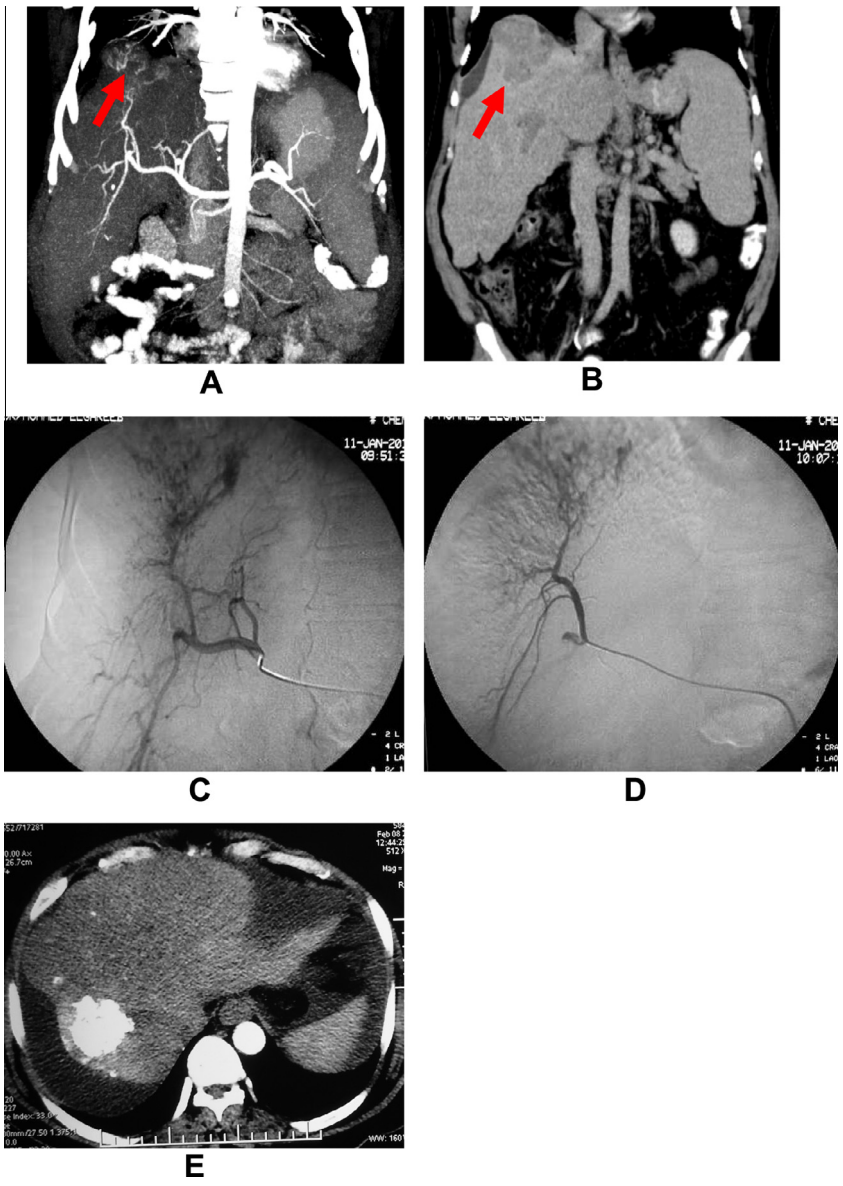


**Fig. 3** Peripheral mild fistula: 47 year old male patient with liver cirrhosis and right hepatic lobe HCC. (A) MIP hepatic arteriogram showing small arterio-portal fistula near the dome of the right lobe (arrow). (B) Coronal reformat at the porto-venous phase clearly demarcates the HCC due to rapid wash out of the contrast (arrow). (C) DSA of the right hepatic artery confirms the presence of the fistula and shunting of contrast to the small peripheral portal vein. (D) Selective catheterization and embolization of the fistula using gel foam particles followed with injection of cytotoxic drug/lipiodol mixture (E). Post chemoembolization of CT scan. The lipiodol is well concentrated within the lesion.

MDCT can perform image data acquisition simultaneously and greatly reduces the time of volume scanning. It offers thin-slice and dynamic enhancement scanning of the liver at early and late arterial phases, and portal venous phase demonstrating clearly the blood supply of the liver and the hemodynamic changes of APS, providing a fast, effective and noninvasive diagnostic method for examination of APS complicating HCC (2).

Clinically, correct interpretation of MDCT findings of HCC associated APS could assist in making right diagnosis and working out effective therapeutic strategy (13).

In our study, MDCT detected 37 APS in 252 HCC patients (14.7%) in near accordance to the findings of Luo et al. (2) as they found 56 APS in 282 HCC patients (19.8%) and the results of Vogl et al. (14) as 7 out of 39 HCC patients (17.9%) had associated APS. MDCT displayed all types and degrees of the thirty-seven APS. Three out of nine (33%) peripheral and mild APS were faint and missed by DSA, very near to the findings of Luo et al. (2) as two out of seven (29%) mild and peripheral APS were missed by DSA.

Depending on data obtained from MDCT, digital subtraction angiograms were performed only for 22 APS patients (out

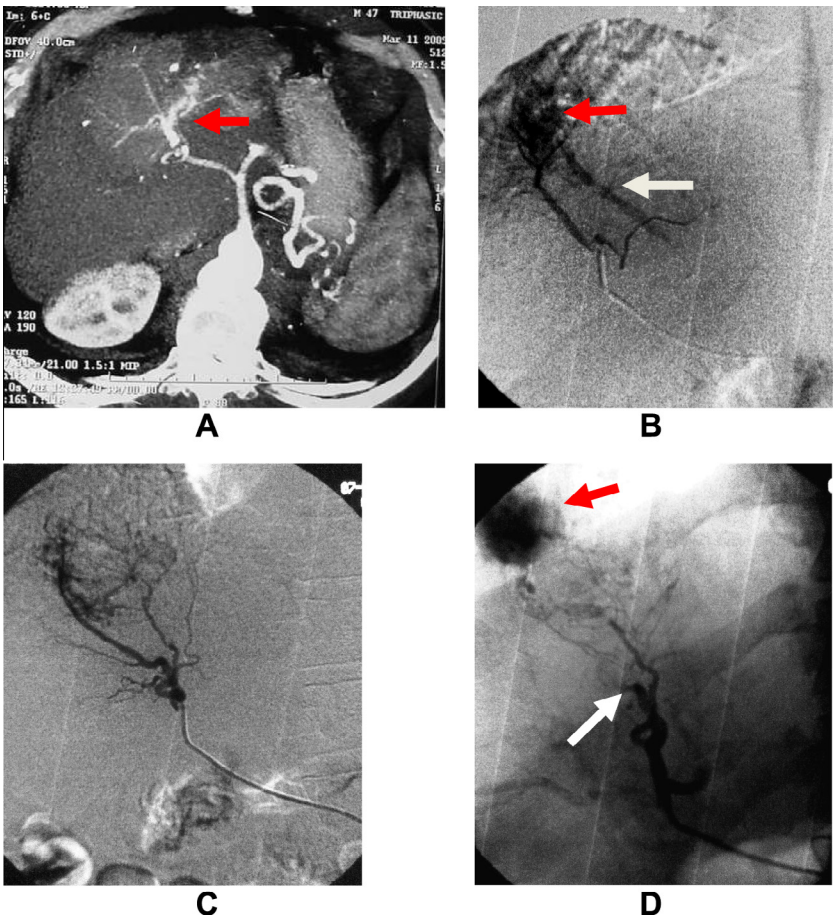


**Fig. 4** Peripheral mild APS: 49 year old female patient with liver cirrhosis and HCC at the lateral segment of the left lobe. (A) Axial MIP at the arterial phase shows shunting of the contrast to the 2nd order branches of the left portal vein (arrow). (B) DSA shows tumor blush (red arrow) and confirms the presence of the APS, with filling of the left portal branch (white arrow). (C) The fistula was embolized using gel foam and cytotoxic lipiodol mixture was injected. (D) The artery involved in the shunt is embolized (white arrow) and the HCC is successfully outlined with lipiodol (red arrow).

of 37) who were candidates for chemoembolization or those suitable for closure of APS by arterial embolization. They included 19 patients without portal venous thrombosis and 3 patients with thrombosis of the distal (peripheral) part of left portal vein.

Seventeen APS were embolized first and then the HCC masses were treated by cytotoxic drug-lipiodol mixture to ensure adequate concentration of the mixture in the tumor. APS was closed only without chemotherapy in one patient just to alleviate the patient's symptoms resulting from complications of the APS. One APS was not closed being mild, peripheral and away from the main bulk of the HCC mass being supplied by another non shunting artery. This HCC mass was treated by cytotoxic drug-lipiodol mixture therapy and then embolizing its feeding artery. Three mild and peripheral APS were missed by DSA.

Fifteen out of thirty-seven patients with APS had thrombosis of the main portal trunk, main right or main left portal veins. These patients were given only liver support as they were not suitable for chemoembolization or closure of the shunts according to the opinion that transarterial chemoembolization has limited value as palliative treatment of cases associated with major portal vein invasion due to the possibility of liver failure following embolization and that it may predispose to hepatic infarction (14). Our multi-disciplinary tumor board coincided also with this opinion regarding these patients.

Materials used for embolization include coils, glue, alcohol, and detachable balloons. For many years, coils were considered the best devices for this indication (15). However, we used gel foam as the main embolizing agent in our cases, due to its availability, low cost and the ability to cut into variable sizes according to the diameter of the target vessel, as the main goal was to ensure good concentration of cytotoxic drug/lipiodol mixture in the tumor and prevent systemic toxicity. The combination of coils and *N*-butyl-2-cyanoacrylate in cases of large fistula has been done by some authors (16,17). In our study we used Hystoacryl in two cases with large fistulas because of its good penetration, dispersion that is freer than that for other embolizing materials, and rapid induction of thrombosis and permanent occlusion after

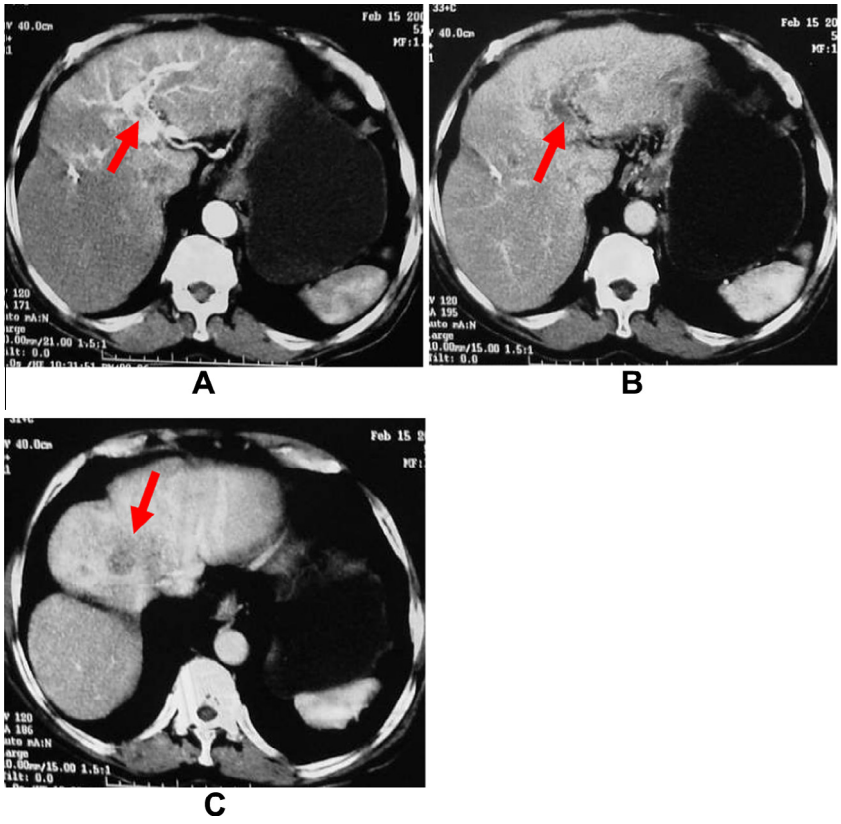


**Fig. 5** Mixed severe APS: 75 year old male patient with liver cirrhosis and nodular HCC at segment IV of the relatively hypertrophied left lobe. (A) Axial CT cut at the arterial phase shows enhancement of the left portal veins as far as the 2nd order branches, with ill defined intra-luminal filling defect at the left main portal vein (red arrow). (B) Partial thrombosis of the left portal vein is confirmed at the portal venous phase (arrow head). (C) The HCC is better seen at the venous phase due to wash out of the contrast (arrow).

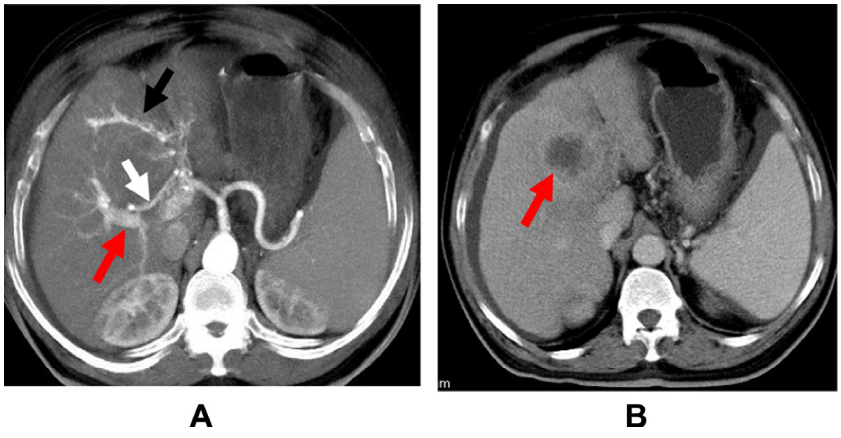


**Fig. 6** Mixed moderate APS: 55 year old male patient with liver cirrhosis and nodular HCC at segment IV of the left lobe. (A) Axial MIP image at the late arterial phase shows enhancement of the right main portal vein (red arrow) as well as the 2nd order branches of the left portal vein (black arrow), with non obstructing thrombus at the right portal vein (white arrow) (B) The HCC is seen at the porto-venous phase with central necrotic core (arrow). Medical liver support was considered for the patient.

polymerization when exposed to ionic medium such as blood or saline. Although non-target embolization can occur, we found it safe and effective for treating fistulas as we embolized only abnormal vessels. No significant complications related to embolization were encountered during the course of the study.

**Fig. 7** Mild peripheral APS: 50 year old male patient with wedge-shaped enhancement peripheral to HCC (arrows). The patient was referred for selective chemoembolization.

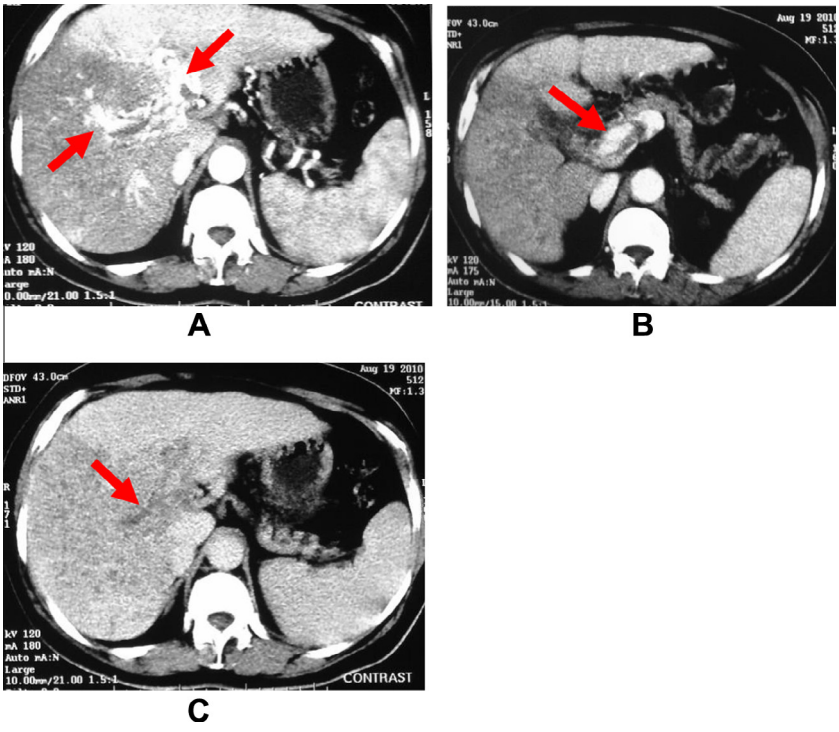


**Fig. 8** Central APS with portal venous thrombosis: 57 year old male patient with liver cirrhosis and diffuse neoplastic infiltration of the right lobe. (A) Axial CT at the arterial phase shows intense enhancement of the right and left portal veins (red arrows) with differential enhancement of the right and left lobes (B) Non-obstructing mural thrombus is present at the main portal vein (arrow) (C) The right portal vein shows tumoral thrombosis (arrow). The hypodensity of the right lobe reflects an element of infarction. No interventional procedure was done and further management was carried out by medical liver support.

## 5. Conclusion

Triphasic thin-slice MDCT is an effective and noninvasive technique that could diagnose the different types and degrees of HCC-associated APS in our study. Good understanding of MDCT findings of these shunts warranted closure of the shunt during the chemoembolization procedure in many patients to improve the therapeutic outcome and avoid escape of the embolic agent to non-tumoral parts of the liver.

## 6. Conflict of interest

The authors have no conflict of interest to declare.

## 7. Funds, sponsorship or financial support

None declared.

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